REMARKS

Support for the Amendment

Support for the amendments to the claims are discussed below with regard to the 35 U.S.C. § 112 rejections, thus no new matter has been added.

Status of the Claims

Claims 1, 2, 7, 14-17, 26, 30, 31, 33, 45, 61, 65, 68, and 74-85 are pending. Claims 1, 30, 45, 61, and 82 are amended.

Request for Reconsideration

Applicants' independent device claims are directed to sensor strips specifying an organic mediator at a first electrode and both redox species of a metal complex mediator at a second electrode. Applicant's independent method claim uses a sensor strip having an organic mediator at a first electrode and a metal complex mediator at a second electrode where a substantially linear correlation between current and analyte concentration is obtained from zero to about 400 mg/dL.

None of the cited references, alone or in combination, teach or in any way suggest that two different types of mediators (organic v. metal complex) should be used on two or more different electrodes of the same sensor strip. Neither can a teaching to the possible substitution of a metal complex mediator with an organic mediator make obvious the separate use of both of these different types of mediators at the different electrodes of the same sensor strip.

While the office action appears to assert that *Kuhn* and/or *Taniike* teach the use of different mediators simultaneously, this position would be inconsistent with the teaching of the references as a whole. *Winarta* and *Taniike* disclose one redox species of a single mediator. *Kuhn* discloses two redox species of a single mediator. Thus, the references disclose the potential substitution of one mediator with another, not the use of two different mediators simultaneously on the different electrodes of the same sensor strip.

The 35 U.S.C. § 112 Rejections are Moot

Claim 30 was amended to include the word "soluble" to correct antecedent basis. Claims 45 and 82 were amended to correct claim dependency. Claims 1 and 61 were amended to substitute "substrate" with "analyte" as intended. Claims 1 and 61 are now consistent with the definitions in the specification and the language of the claims depending from claims 1 and 61. Thus, the rejections of claims 30, 35, 61, and 82 under § 112 are believed to been rendered moot by appropriate amendment. Applicants thank the Examiner for pointing out these errors. In view of the amendment made to claim 45 and the Examiner's comments, Applicants believe claim 45 is in condition for allowance.

Claim 85 was rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicant believes claim 85 to be definite as written. The office action states that the 0 to 600 mg/dL range of claim 85 is broader in scope than the 0 to 400 mg/dL range of claim 61. While the numerical range of 0 to 600 is broader than 0 to 400, from a claim scope perspective 0 to 600 is narrower than 0 to 400. This is because in the context of the claim it is more difficult to provide substantially linear correlation over the numerically broader 0 to 600 range than to provide substantial linearity over the numerically narrower 0 to 400 range. While counterintuitive, a method meeting the 0 to 600 mg/dL range would meet the limitation of a 0 to 400 mg/dL range; however, a method meeting the 0 to 400 mg/dL range may or may not meet the 0 to 600 mg/dL range. Thus, the scope of claim 61 is narrowed by the 0 to 600 mg/dL range of claim 85 in relation to the broader requirement of the 0 to 400 mg/dL range of the independent claim. The rejection of claim 85 under § 112 is believed to have been rendered moot by appropriate explanation. Applicants' representative would gladly discuss this distinction with the Examiner if additional clarification is needed.

Claims 79, 80, and 84 were rejected under 35 U.S.C. § 112, first paragraph, as failing to be supported by sufficient written description. Applicant respectfully

traverses this rejection with regard to these claims. Each of these claims limits the reagents deposited at the first electrode (first reagent layer) or at the second electrode (second reagent layer) so that "the electroactive organic molecule and the oxidoreductase is substantially present only in the first reagent layer, and the soluble redox species is substantially present only in the second reagent layer". Thus, the limitation of these claims is intended to limit the claim to the situation where there is substantially no mixing of the reagents at the first electrode (organic molecule and oxidoreductase) with the reagents at the second electrode (soluble redox species of a metal complex).

There are multiple instances where the benefits of such reagent separation are described in the specification. For example, paragraph [0046] describes the benefits of the two electrodes having different reagents, which allows for separate optimization of the electrical and other properties of the working and counter electrodes. In paragraph [0069] of Example 2 the strip was formed by depositing the enzyme (the oxidoreductase for this example) and PIPT (the electroactive organic molecule for this example) on the working electrode (first electrode for this example), while only ferricyanide (the soluble redox species of the metal complex mediator for this example) was deposited at the other electrode (second electrode for this example). Thus, the claim language directed to the substantial separation of the reagents between the first and second electrodes is believed supported by the general text of the application and by specific example. The rejection of claims 79, 80, and 84 under § 112, first paragraph, is believed to have been traversed by indentifying support in the specification.

The rejections under § 112 are believed to have been rendered moot by appropriate amendment/explanation or traversed; withdrawal of the rejections is respectfully requested.

The Claims are Not Anticipated by or Obvious Over the Cited Art

Applicant notes that the prior rejections under 35 U.S.C. § 102 over U.S. Pat. No. 6,287,451 ("*Winarta*") have been overcome.

The rejection under 35 U.S.C. 103(a) of claims 1, 2, 7, 14-17, 26, 30, 31, 33, 61, 65, 68, and 74-85 as being obvious over U.S. Pat. No.6,287,451 (D1) ("*Winarta*") in view of U.S. Pat. No. 5,385,846 ("*Kuhn*") and/or U.S. Pat. Pub. No. 2001/0006149 ("*Taniike*") (D2), and further in view of *Morris* (D4) or U.S. Pat. No. 5,520,786 ("*Bloczynski*") (D7) is respectfully traversed.

Teachings of The Applied References

Winarta teaches a sensor strip having working and counter electrodes made from the same reagent composition, except that the counter electrode lacks an enzyme. Col. 8, Lines 37-47. Thus, the enzyme is present only at the working electrode. The same oxidized form of a single redox mediator (potassium ferricyanide) is used in the reagent composition for both electrodes ("Reagents 1 and 2 comprise the oxidized form of a redox mediator..."). Col. 9, Lines 15-19. This formulation also is described in Col. 10, Lines 44-46 and Lines 53-56, where only potassium ferricyanide is included in the reagent compositions. Thus, *Winarta* teaches that the oxidized (thus reducible) redox species (potassium ferricyanide) of a single metal complex mediator is present at both the working and counter electrodes, with the difference between the electrodes being that an enzyme is present at the working electrode, but not at the counter electrode.

Kuhn teaches a sensor capable of measuring how one or more components of a sample (the reference addresses red blood cells in whole blood) are affecting the diffusion of one species of a redox pair (ferrocyanide) to a working electrode to be oxidized while the other species of the same redox pair (ferricyanide) is being reduced at the counter electrode. Col. 4, Lines 13-22. Both species of the redox pair of a single mediator cover both electrodes. Col. 3, Lines 21-23; Figure 2; Col. 4, Lines 13-15. The quantity of the species of the redox pair measured at the working electrode

(ferrocyanide) must be sufficient when the sensor is made to not limit current during the analysis. Col. 4, Lines 33-36, 53-56, 60-63. Unless insufficient or an undesirable overage of ferrocyanide is present, the differences in current measured by the device correlate to the degree to which the components of the sample (red blood cells) interfere with the diffusion of the ferrocyanide to the working electrode of the sensor during the analysis, not to the concentration of an analyte responsive mediator in the sample. Col. 4, Lines 30-33, 53-68 through Col. 5, Lines 1-15. Thus, *Kuhn* determines the effect that a diffusion affecting species has on the measurement of a species of a redox pair (ferrocyanide) that is present on the strip at the time of manufacture. *Kuhn* also teaches that an electroactive organic molecule may be used in place of the single metal complex mediator to provide the two species of the redox pair. Col. 5, Lines 64-67.

Taniike teaches sensor strips where the enzyme is present at the working electrode, but not at the counter electrode, and where a ferricyanide mediator is present at the counter electrode, but not at the working electrode. Para. [0050]. Thus, each of the examples in *Taniike* describe a sensor strip where an enzyme, but no mediator, is deposited at the working electrode, while a single mediator, but no enzyme, is deposited at the counter electrode. *Taniike* also teaches that an electroactive organic molecule may be substituted for the ferricyanide mediator at the counter electrode. Para. [0036] and [0030].

Morris teaches that ruthenium (III) hexamine may be used as an alternate to potassium ferricyanide as a redox mediator. Pg. 2, Para. 1. *Bloczynski* teaches the use of 3-phenylimino-3H-phenothiazine and 3-phenylimino-3H-phenoxazine as electrochemical mediators.

Obviousness

Independent claims 1 and 30 specify that a first electrode includes an electroactive organic molecule and an oxidoreductase and that a second electrode includes both species of a soluble redox pair in a range of ratios. The soluble redox pair is provided by a metal complex, being either an OTM or a coordination complex or a mixture thereof. Thus, a single sensor strip includes an organic mediator at a first electrode and both redox species of a metal complex mediator at a second electrode.

I. The cited references do not teach organic and metal complex mediators at different electrodes of the same strip.

None of the cited references include or in any way suggest that one electrode of a sensor strip should include an organic mediator while another electrode of the same strip should include both species of the redox pair of a metal complex mediator. *Winarta* teaches that a sensor strip should use one redox species of a single metal complex mediator at both the working and counter electrodes. *Taniike* teaches that a sensor strip should use one redox species of a single metal complex mediator at the counter electrode and that only an enzyme should be present at the working electrode. *Kuhn* teaches that a sensor strip should include both redox species of the redox pair of a single metal complex mediator on both electrodes. Unlike stated in the office action, *Kuhn* does not teach that multiple mediators should be used simultaneously, but instead teaches that the two redox species (ferrocyanide and ferricyanide) of the redox pair of a single mediator should be used on both the working and counter electrodes. None of the references alone or in combination teach or suggest that two different types of mediators should be segregated on different electrodes of the same sensor strip, as specified in each of Applicants' independent claims.

II. *Kuhn* is not properly combinable with *Winarta* and *Taniike*.

Kuhn lacks an enzyme which transfers electrons from an analyte to one of the redox species of a mediator, thus Kuhn lacks the ability to generate a redox species concentration in the sample responsive to the analyte concentration of the sample. *Kuhn* may not be combined with *Winarta* and *Taniike* as the concentration of the redox species measured at the working electrode of *Kuhn* was not formed from the analyte, but is provided when the strip is made. In fact, if the teaching of ferrocyanide at both the working and counter electrodes of *Kuhn* were combined with *Winarta* and *Taniike,* a device unsatisfactory for its intended purpose would result as there would be no way to determine the concentration of the glucose analyte with which the enzymes of *Winarta* and *Taniike* interact from the redox species applied during manufacture. References are not properly combinable when their combined teachings result in a device unsatisfactory for its intended purpose because there could be no motivation or suggestion to make such a modification. MPEP § 2143.01(V).

III. The claimed inventions are not obvious from the improper combination.

Even if improperly combined, the combination of *Kuhn* with *Winarta* and *Taniike* would not have made the invention of the claims obvious as the use of two different mediators on the different electrodes of a strip is not suggested or motivated. *Winarta* provides a sensor strip having one redox species of a single metal complex mediator at both the working and counter electrodes while the enzyme resides at the working electrode. The combination of *Taniike* with *Winarta* would apparently require the removal of the redox species from the working electrode as *Taniike* teaches a mediator only on the counter electrode. The combination of *Kuhn* with this strip would presumably require the replacement of the one redox species of a single mediator with both redox species of the single mediator at the counter electrode and the deposition of both redox species of the single mediator at the working electrode. The elements of such a "combination strip" are indeterminable as these combinations would provide a device or method unsatisfactory for its intended purpose.

Even using Applicants' claims as a guide, the closest the combination of the cited references can apparently come to suggesting the present claims is a sensor strip having only an enzyme at the working electrode and both species of the redox pair of a single mediator at the counter electrode. This strip fails to make Applicants' claims obvious as Applicants' claims also specify a different mediator at the working electrode in relation to the mediator used at the counter electrode. Absent a teaching to pick different mediators and deposit them on different electrodes of the same sensor strip, such a construction cannot be obvious as there is no motivation or suggestion to try such. In fact, such a construction would not be considered in view of the cited references due to the mismatch in electrical properties between the resulting electrodes. Regardless of how the cited references are combined, the invention of Applicants' claims 1, 30, and 61 will not result and cannot be made obvious as only sensor strips using a single mediator, whether metal complex or substituted with an organic, can result from the cited references when reviewed as a whole.

IV. A teaching to the possible substitution of a metal complex mediator with an organic mediator provides no teaching or motivation to segregate two different types of mediators on different electrodes of the same strip.

Taniike and *Kuhn* teach that organic mediators may be substituted for metal complex mediators. The fact that one metal complex mediator may be replaced with another metal complex mediator or with an organic mediator provides no suggestion that two chemically and electrochemically different types of mediators could be used successfully on different electrodes of the same sensor strip or that any benefit would arise from doing such. For example, and as stated in the office action, *Taniike* teaches that electroactive organic molecules, including p-benzoquinone, may be used as an electron mediator. Par. [0036]. *Taniike* also teaches that potassium ferricyanide mediator (a transition metal coordination complex in the context of Applicants' claims) only should be present at the counter electrode. Par. [0042]. Thus, unlike Applicants' claims which specify a metal complex mediator at the counter electrode and an

organic mediator at the working electrode, *Taniike* teaches that the metal complex mediator at the counter electrode may be substituted or combined with an organic mediator at the working electrode – nothing more. *Kuhn* teaches that organics can be "used in place of" ferricyanide, and thus under *Kuhn* both redox species of the single organic mediator substituted for the metal complex mediator would be deposited at both electrodes. Col. 5, Lines 63-65. As in *Taniike*, only a substitution of one type of mediator with another type of mediator is suggested, not the use of two different types of mediators, each on a different electrode, as specified by Applicants' claims.

V. A reference teaching a linear performance for one type of analysis provides no teaching regarding the linearity performance of an unrelated analysis.

Method claim 61 specifies a method where the correlation between the current and the concentration of the analyte is substantially linear from zero to an analyte concentration of about 400 mg/dL for a sensor strip using an organic mediator at a first electrode and a metal complex mediator at a second electrode. However, the difference in the redox potentials of the organic mediator at the working electrode versus the metal complex mediator at the counter electrode creates an electrical imbalance that would have been expected to provide poor linearity in the correlation performance of such a sensor strip. Hence, Applicants' claimed linearity is unexpected. While Applicants' agree with the Examiner that *Winarta* teaches a 35 to 1000 mg/dL correlation between current and analyte concentration (Col. 14, Lines 25-28), such a correlation cannot make the claimed range obvious as the range of *Winarta* was not obtained from a sensor strip having different mediators at the working and counter electrodes (*Winarta* uses ferricyanide at both electrodes). Being from a very different device, the *Winarta* range cannot make the range of claim 61 obvious.

VI. "Prior to the use of the sensor strip in an analysis" does not introduce a "use" under MPEP § 2144.

Applicant is confused regarding the Examiner's characterization of the limitation "prior to use of the sensor strip in an analysis" as a manner of use. This limitation was

added to specify that the electrochemical sensor strip being claimed is as it exists before a sample is added and the analysis performed – as the ratio of the redox species will change during the analysis. Thus, the limitation has no bearing on use and does not introduce a "use" as defined under MPEP § 2144 into the claim. This limitation was added for the sole purpose of speeding prosecution by explicitly stating what was already inherent to the claims in view of the specification; that the strip being claimed is the strip as it exists at the time of manufacture and before use in an analysis. The remaining statements on page 7 of the office action also contain statements that are technically incorrect with regard to the operation of Applicants' strip as the statements appear to be based on the operation of the strip described in *Kuhn*. As previously described, the sensor strip of *Kuhn* operates in a manner unrelated to Applicants'. However, in view of the statement on page 8 of the office action that "Winarta et al fails to disclose the use of two mediators placed in the reagent prior to use and explicitly teach the molar ration of these two redox species", Applicant does not believe the statement regarding § 2144 nor the technical statements that follow to be at issue.

The rejections of claims 1, 30, and 61 should be withdrawn because the invention defined by the claims would not have been obvious in view of the cited art because even if properly combinable and a motivation to combine the references existed, the resulting sensor strips and methods of operation fail to provide or render the claimed inventions obvious. Thus, the Applicants' respectfully request that the rejections under 35 U.S.C. § 103(a) of independent claims 1, 30, 61 and their respective dependent claims be withdrawn as the above remarks regarding the independent claims apply equally to the dependent claims.

Conclusion

The Applicant believes the Examiner's concerns have been addressed to overcome the rejections. Upon the indication of allowable subject matter, the Examiner is respectfully requested to telephone Jonathan M. Blanchard at 312-612-

6700 to resolve any outstanding issues as expeditiously as possible so the case may be passed to issue.

Respectfully Submitted,

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Date

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